GENERAL INVESTIGATIONAL PLAN

EBV-specific CTLs are generated by coculturing peripheral blood mononuclear cells with irradiated lymphoblastoid cell lines. All cells are autologously derived and the CTLs will be transduced with clinical grade G1Na vector supplied by Genetic Therapy Inc.

The objectives of the proposed study relate to the safety and immunologic and virologic efficacy of EBV-specific CTLs in a patient population with relapsed EBV-positive Hodgkin disease. Gene-marking the CTLs allows us to monitor the survival of the transferred cells and does not confer any therapeutic advantage or disadvantage. The proportion of NeoR positive cells will be determined by semi-quantitative PCR as previously published by us and others. This will allow us to determine the kinetics of CTL survival and allow us to learn if any expansion occurs in vivo. Long term follow up for issues relating to the safety of gene marking will be the responsibility of St Jude Children's Hospital.

The efficacy of EBV-specific CTLs will be measured by assessing:

1) The longevity of infused CTLs in peripheral blood by amplification of the NeoR gene.

2) The immunophenotype of PBLs to determine how the CTL infusion influences circulating lymphocyte subsets.

3) The cytotoxic effector function of peripheral blood lymphocytes pre and post infusion of EBV-specific CTLs to evaluate their ability to eradicate tumor cells.

4) Changes in Tcell repertoire usage to detect expansion of effector cell subsets.

5) Changes in levels of EBV DNA in peripheral and mucosal compartments to monitor the effects of CTL therapy on the recipient virus load.